REMARKS

Claim Amendments

Claims 36-53 are currently pending in this application. Claims 36-39, 44-49 and 51-52 are currently amended herein. Claims 43 and 50 are cancelled herein without prejudice or disclaimer as to the subject matter disclosed therein. New claims 54-66 are presented for entry and consideration. Accordingly, upon entry of this amendment, claims 36-42, 44-49 and 51-66 will be pending. Support for the amended and new claims is found throughout the application as originally filed.

Claim 36 has been amended to recite oilseed rape, *Arabidopsis* or corn. Claim 36 has also been amended to delete the term "about." Furthermore, claim 36 has been bifurcated to better reflect that dsRNA encoding chimeric genes based on corn PARP genes (SEQ ID Nos: 1, 3 or 10) are intended for use in corn, whereas dsRNA encoding chimeric genes based on PARP genes from *Arabidopsis* are intended for use in Brassicaceae species (oilseed rape, *Arabidopsis*). Support for amended claim 36 is found, for example, on pages 28 and 29 and Examples 4 and 5 in the specification as filed. Dependent claims 37-39, and claims 44-48 drawn to transgenic plants, have been amended in a corresponding manner. Claim 49 has been amended to correct a typographical error to properly refer to a "transgenic plant" rather than to a "method," and has been amended to refer to the independent claim 44, rather than dependent claim 47. The dependency of claim 51 has also been corrected. Claim 52 has been amended to delete the term "about."

Support for new claim 54 is found, for example, in the paragraph spanning pages 20 and 21. Support for new claim 55 is found, for example, on page 21 read in conjunction with the identification of the nucleotide sequence encoding the PARP signature on page 17.

The nucleotide sequence recited in claim 55 for SEQ ID No: 10 finds support at least on page 21, lines 11 to 15, which teaches that sense or antisense sequences may comprise a nucleotide sequence of at least 100 consecutive nucleotides encompassing the PARP signature. The location of the PARP signature spans from amino acid position 827 to 875 of the ZAP2 protein of SEQ ID No. 11. *See e.g.*, page 15, lines 14-15. The amino acid sequence of SEQ ID No. 11 is encoded by the nucleotide sequence of SEQ ID No: 10. *See e.g.*, page 29. In the sequence listing, SEQ ID No. 10 shows both the nucleotide sequence and the encoded protein, each with their own numbering. Accordingly, the nucleotide sequence of position 2559 to 2705

of SEQ ID No. 10 can be directly correlated with the encoded amino acid sequence of 827 to 875 of the ZAP2 protein.

Support for the recitation of a minimum length of 250 or 500 nucleotides is found, for example, on page 19. New dependent claims 58-61 and 62-65 mirror claims 54-57 discussed above. Support for new claim 66 is found, for example, on pages 20, 21 and 24.

No new matter is added as result of this amendment. Applicants reserve their right to file a continuation or divisional application directed to the subject matter cancelled without prejudice or disclaimer by the current amendment.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

Claims 36-53 Deemed Free of the Prior Art

Applicants appreciate the Examiner's recognition that claims 36-53 are deemed free of prior art for the reasons set forth on page 7 and 8 of the Office Action.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 36-53 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement.

In making this rejection, the Examiner states that a sense or antisense nucleotide sequence comprising a nucleotide sequence "of about 100" consecutive nucleotides from a nucleotide sequence selected from the group consisting of the nucleotide sequence of SEQ ID No. 1, the nucleotide sequence of SEQ ID No. 3, the nucleotide sequence of SEQ ID No. 5 or the nucleotide sequence of SEQ ID No. 10 (or the complement thereof) does not find support in the specification as filed and thus constitutes new matter.

Applicants have amended the claims to delete the recitation of "about." In view of this amendment, Applicants respectfully request reconsideration and withdrawal of this rejection.

To the extent this rejection applies to the amended or new claims, it is respectfully traversed. Support for the term "about" is found throughout the specification. *See e.g.*, pages 20, 21 and 24.

Claims 36-53 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement.

In making this rejection, the Examiner acknowledges the teaching of the specific Examples in the specification, but maintains that the claimed invention is not enabled because making and using double stranded RNA molecules that can produce a specific phenotype in a particular type of plant cell is unpredictable. The Examiner cites to Fire et al., Bosher et al., Wang et al. and Helliwell et al. to support this assertion.

Applicants respectfully disagree and traverse this rejection.

Applicants have for the first time described that downregulation of PARP genes through dsRNA mediated gene silencing leads to an increase in the vigor of plants. The specification provides the specific nucleotide sequences of SEQ ID NOS: 1, 3, 5 and 10 useful to achieve this goal. The specification teaches the construction and transformation of dsRNA chimeric genes. *See e.g.*, Examples 3-5. The specification further teaches an *in vitro* assay to test vigor of several plant lines. *See e.g.*, Example 6. Furthermore, as the Examiner recognizes, the specification demonstrates that for *Arabidopsis thaliana* and *Brassica napus* plants comprising combinations (APP/ZAP) of PCD modulating genes under control of a CaMV35S or NOS promoter, a high vigor is observed in a number of transgenic lines. *See e.g.*, Office Action at page 4 and Example 7. Accordingly, Applicants assert the specification teaches one of skill in the art how to make and use the claimed invention.

The Examiner cites to Fire et al. and Bosher et al. to show that injection into *C. elegans* of double stranded RNA directed to different parts of a gene results in different phenotypes. The Examiner does not, however, provide any evidence that such results in *C. elegans* can be extrapolated to claimed invention.

Nevertheless, to rebut the Examiner's implied assertion that dsRNA encoding a chimeric gene targeting different parts of the PARP genes would result in different phenotypes, Applicants submit herewith Dr. Marc De Block's Supplemental Declaration ("Supplemental Declaration"), previously submitted during prosecution of the parent application (Ser. No. 09/118,276), attached as **Exhibit A**, and Dr. Marc De Block's Second Supplemental Declaration ("Second Supplemental Declaration") and its accompanying publication in The Plant Journal ("the publication"), attached as **Exhibit B**.

The publication includes data presented in the Supplemental Declaration on the *Arabidopsis* and *Brassica* plants comprising the dsRNA chimeric genes of the invention. The chimeric genes described in the publication as *htAtParp1* correspond to the chimeric gene indicated in the Supplemental Declaration as pTYG48. *See e.g.*, Second Supplemental

Declaration at paragraph 6(c). The chimeric genes described in the publication as *htAtParp2* correspond to the chimeric gene indicated in the Supplemental Declaration as pTYG29. *See e.g.*, Second Supplemental Declaration paragraph 6(d). *htAtParp1*and *htAtParp2* target the N-terminal part the *parp1* gene (previously indicated as ZAP) or *parp2* (previously indicated as *app*), respectively, as can be seen from the description of the constructs in the "Experimental procedures/Plasmid constructs" section on page 103 left column of the publication. *See also* Second Supplemental Declaration at paragraph 7.

The publication discloses a third chimeric gene construct *htAtParp2(signature)* that targets the PARP signature located in the C-terminal part of the *parp*2 gene. *See* Second Supplemental Declaration at paragraph 8. This chimeric gene was also successfully used to obtain stress-resistant, vigorous plants. *See e.g.*, publication at page 97 and Second Supplemental Declaration at paragraph 9.

Accordingly, chimeric genes targeting different parts of the PARP genes located in N-terminal or the C-terminal part can both be used to obtain more vigorous plants. *See* Second Supplemental Declaration paragraph 10.

The Examiner cites to Wang et al. to show that in plants introns seem to be poor targets for posttranscriptional silencing and that silencing appears to be most efficient when sequences of more than 300 base pairs are used.

Applicants respectfully submit that it is irrelevant for the claimed invention whether introns seem to be poor targets for posttranscriptional silencing. All nucleotide sequences recited in the claims are **cDNA** sequences and do not contain introns. *See also* Example 1. Chimeric genes encoding dsRNA which contain sense and antisense nucleotide sequences selected from the recited nucleotide sequences accordingly do not target introns.

Applicants respectfully submit the statement that silencing appears to be most efficient when sequences of more than 300 base pairs are used, is not tantamount to a statement that shorter fragments do not work, only that they may not be as efficient. For example, the Second Supplemental Declaration and the publication demonstrate that a shorter dsRNA fragment of about 158 bp as in *htAtParp2(signature)* can be used to obtain the vigorous plants according to the invention. *See* Second Supplemental Declaration at paragraph 11.

The Examiner cites to Helliwell et al. for the proposition that shorter gene fragments result in lower frequency of gene silencing and that gene silencing appears to be gene dependent.

As indicated above, with respect to Wang et al., the experimental data indicates that shorter dsRNA fragments may be used for PARP genes. Furthermore, while it may be true that gene silencing appears to be gene dependent, the claimed invention is specifically directed to gene silencing of PARP genes.

On pages 6 and 7 of the Office Action, the Examiner states that the specification does not provide sufficient guidance with respect to which of the recited RNA molecules to express and in what type of plant cell to produce a plant cell that has high vigor.

The question of which RNA molecules to express has been addressed above. Regarding the type of plant cell in which to express these RNA molecules, the claims have been amended to recite oilseed rape, *Arabidopsis* or corn. Furthermore, the evidence provided in the Supplemental Declaration, Second Supplemental Declaration and the publication make clear that the claimed invention may be applied to oilseed rape, *Arabidopsis* and corn. *See e.g.*, Second Supplemental Declaration at paragraphs 10 and 13-15.

In view of the above arguments, Applicants respectfully request withdrawal of the enablement rejection.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 36-39, 44-48 and 52 and claims dependent thereon have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite in the recitation of "of about 100."

Applicants respectfully assert the deletion of the term "about" renders this rejection moot.

CONCLUSION

Applicants respectfully submit that claims 36-42, 44-49 and 51-66 are in condition for allowance, and such disposition is earnestly solicited. Should the Examiner believe that any issues remain after consideration of this Response, the Examiner is encouraged to contact the Applicant's undersigned representative to discuss and resolve any such issues.

Respectfully submitted,

HUNTON & WILLIAMS LLP

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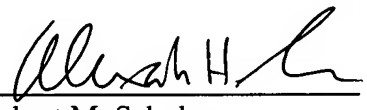
By: 

Robert M. Schulman
Registration No. 31,196

Alexander H. Spiegler
Registration No. 56,625

HUNTON & WILLIAMS LLP
Intellectual Property Department
1900 K Street, N.W., Suite 1200
Washington, D.C. 20006
(202) 955-1500 (telephone)
(202) 778-2201 (facsimile)
RMS/JLP/cdh